REMARKS

The Office Action and the cited and applied reference have been carefully reviewed. Claims 7-9 are allowed. Claims 1-9, 11, and 14-17 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 3-6 and 11 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. This rejection is respectfully traversed.

Claim 3 has been amended to clearer define the variant with physicochemical properties (1) to (4) and amino acid sequence. It should be noted that replacement, deletion and addition of at least one amino acid residue are made so as to not substantially alter biological activity (3), i.e., "inducing the interferon-gamma production by immunocompetent cells". In other words, if replacement, deletion and addition of at least one amino acid residue made to obtain a variant substantially alters biological activity (3), then such a variant is not covered by claim 3.

Applicant believes that a protein of claim 3 is clearly defined by the preamble where recitation of "a purified interferon-gamma production inducing protein, which is a variant of an interferon-gamma production inducing protein, also known as

IGIF and IL-18". It is believed that the metes and bounds of "a variant of a protein known as IGIF and IL-18" are clear and easily understandable to a skilled artisan.

A factor disclosed in the Nakamura et al. reference, INFECTION AND IMMUNITY, vol.61, no.1, pp.64-70 (1993), cited and applied by the examiner, does not satisfy the molecular weight (1) limitation and therefore is excluded from claim 3.

Furthermore, the applicant again emphasizes that the metes and bounds of "a sequence variant of SEQ ID NO:2" is clear to a skilled person. As support, copies of the following two publications are attached hereto:

1. *Concise Encyclopedia Biochemistry*, Second Edition, pp.385-386 (1988)

2. *Recombinant DNA, A Short Course*, edited by James D. Watson et al., pp.106-116 (1983)

The attached pages of the *Concise Encyclopedia Biochemistry* states that there are mutations at the gene level in the genetic material of a cell or organism. The attached pertinent section of *Recombinant DNA* states that it is easy for a skilled person to obtain a variant of a molecule encoded by a DNA (corresponds to "a sequence variant of SEQ ID NO:2"). These two publications are considered to constitute the state of the art at the time the present application was filed. It is therefore believed that a person having ordinary skill in the art would easily understand what is meant by "a sequence variant of SEQ ID NO:2". In view of

above, applicant believes that the metes and bounds of claim 3 can be determined and are therefore clear.

The examiner also stated that "the N-terminal region" is indefinite because the examiner questions up to what length from the N-terminus is still considered "the N-terminal region". In response, claim 3 has been amended to replace "the N-terminal region" with "SEQ ID NO:2".

It is further said that the recitation "an amino acid sequence of SEQ ID NO:2" is indefinite because the term "an" indicates more than one sequence in SEQ ID NO:2. The examiner helpfully suggests replacing the term "an" with "the" and this suggestion is now adopted.

The recitation "physicochemical property (3) is amended to "biological activity" as "biological activity" is already recited in claim 3.

The examiner further states that claim 11 is indefinite because it is unclear what "the same antigenic fragments" are, and whether the sequence variant have to retain any property other than "antigenic fragment". It should be noted that "the same antigenic fragments" means "antigenic fragments" inherent to the protein having the amino acid sequence of SEQ ID NO:2. Applicant has deleted the term "same" before "antigenic fragments" in claim 11 to make more definite what is meant by the recitation. It is believed that it has also become clear whether

or not the sequence variant have to retain any property other than "antigenic fragment".

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 3-6 remain rejected under 35 U.S.C. §112, first paragraph, because the examiner holds that the specification, while being enabling for claims limited in scope to a specific variant of said protein, which has an amino acid sequence of SEQ ID NO:2 where residue 70 is methionine or threonine, does not reasonably provide enablement for claims to variants having physicochemical and functional properties listed in parts (1) to (4) of claim 3, and having the amino acid sequence of SEQ ID NO:2 with at least one amino acid residue in SEQ ID NO:2 replaced with different amino acid or at least one amino acid residue deleted or added to the N-terminus of SEQ ID NO:2 while not substantially altering the physicochemical properties of the protein.

Claims 1, 2, 11, 14 and 15 also remain rejected, and the new claims 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the examiner states that the specification, while being enabling for claims limited in scope to a protein with SEQ ID NO:2, wherein residue 70 is methionine or threonine, does not reasonably provide enablement for any IL-18 (claims 1, 2, 16 and 17, for example) or variants with proteins listed in

these claims (claims 11, 14 and 15, for example). These two rejections are respectfully traversed.

As discussed above regarding the indefiniteness rejection, the applicant believes that it would have been easy for a skilled person to obtain "a sequence variant of SEQ ID NO:2" once the amino acid sequence of SEQ ID NO:2 is given. Furthermore, it should be noted that claim 3 comprises the limitation of physicochemical properties (1) to (4). Applicants therefore believe that the specification does reasonably provide enablement for "a sequence variant of SEQ ID NO:2" when the state of the art is taken into account.

Also as discussed above regarding the indefiniteness rejection, one of skill in the art would be able to obtain "a sequence variant of SEQ ID NO:2" with only routine experimentation once the amino acid sequence of SEQ ID NO:2 is given and the state of the art is taken into account. Applicants believe that the claims should not be restricted to what is disclosed in the examples. Furthermore, a protein as defined in the rejected claims are encompassed within the category of "IGIF or "IL-18", which are established technical terms, and have the specified physicochemical properties, such as molecular weight, isoelectric point, and biological activity. Such proteins had not been known before the present invention was made. In this

regard, the present invention is a so-called pioneer invention and should be given relatively wide protection.

Applicants note that the examiner states on page 5, lines 4-6, of the Office Action with respect to claim 11 that "a mAb specific to a sequence variant of the protein" encompasses mAbs specific to the non-common sequences comparing to SEQ ID NO:2 even though the variant shares antigenic fragments of SEQ ID NO:2. However, the examiner's attention is respectfully invited again to the fact that claim 11 comprises limitations other than "a mAb specific to a sequence variant of the protein". The limitation of "a mAb specific to a sequence variant of the protein" is just one of the limitations that define the claimed protein.

The examiner further states that the specification does not disclose any antigenic fragment specific to SEQ ID NO:2. However, this is incorrect. The specification at page 16, lines 4-5, states that a protein having the amino acid sequence of SEQ ID NO:2 has "antigenic fragment(s)."

Reconsideration and withdrawal of the 35 U.S.C. §112, first paragraph, rejections are therefore respectfully requested.

Claims 1-3, 5, 6, 11, 14 and 15 remain rejected, and the new claim 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakamura et al., (Infect. Immun. 61:64-70,

1993), for the reasons set forth in the previous Office Actions, paper Nos. 4, 7 and 13.

The claimed protein is distinct over Nakamura et al. as follows:

(i) The claimed protein has a molecular weight of 19,000±5,000 (i.e. 14-24 kDa) on both gel filtration and SDS-PAGE. By contrast, the factor disclosed in Nakamura has a molecular weight of 70-75 kDa on gel filtration, and 50-55 kDa on SDS-PAGE. In addition to the difference in molecular weight, it can be said that the claimed protein behaves differently from the factor of Nakamura on gel filtration and SDS-PAGE. In other words, the claimed protein is a protein which shows the same molecular weight on both gel filtration and SDS-PAGE, while the factor of Nakamura is a protein which shows different molecular weight on gel filtration and SDS-PAGE.

(ii) Nakamura on page 68, right column, second paragraph, infers that the difference in the determined molecular weight may be caused by the loss of small fragment through gel filtration. This statement in Nakamura suggests that the factor of Nakamura consists of plural factors having different molecular weights.

(iii) The claimed protein retains interferon-gamma production inducing activity even after SDS-PAGE, while the factor of Nakamura loses its activity on SDS-PAGE.

It should again be noted that the claimed protein can be distinguished from the factor of Nakamura in its purity at least as shown in (ii) above, even if the factor of Nakamura comprises the claimed protein. The claimed protein is purified to such a level as to show a single band on SDS-PAGE, while the factor of Nakamura is not so purified because it loses its activity on SDS-PAGE. Nakamura neither recognizes nor separates the claimed protein and Nakamura never discloses the physicochemical properties of the claimed protein. Accordingly, applicants believe that it cannot be considered that the factor of Nakamura is the same protein as the claimed protein.

Reconsideration and withdrawal of the rejections are therefore respectfully requested.

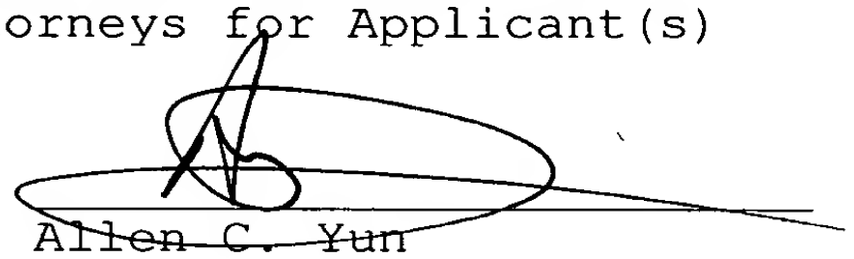
Applicants note that claims 7 to 9 are considered by the examiner to be allowable. Claims 7 to 9, however, relate to a purified protein having the amino acid sequence of SEQ ID NO:2. Applicant believes that claims 7 to 9 are too restrictive as compared with what is disclosed in the specification when the state of the art is taken into account. A skilled person, who has technical common sense such as with regard to what is disclosed in the *Concise Encyclopedia Biochemistry* and *Recombinant DNA* reference, can easily obtain a sequence variant of the amino acid sequence of SEQ ID NO:2 and therefore can easily reduce into practice an invention substantially the same

as one claimed in claims 7 to 9 of the present application without infringing on a patent right established on claims 7 to 9.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and allowance are earnestly urged.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By 
Allen C. Yun
Registration No. 37,971

ACY:pp
624 Ninth Street, N.W.
Washington, D.C. 20001
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
G:\BN\S\SUMA\Okamura2E\pto\Amendment.doc